Discussion

Dr Dirk E. M. Van Raemdonck *(Leuven, Belgium)*. I would like to thank Dr Osaki and colleagues for a clear presentation reporting an in-depth analysis of the late outcomes in a cohort of 18 lung transplant recipients from so-called Maastricht Category III controlled non–heart-beating donors. The LTx group at the University of Wisconsin is to be congratulated with this largest and longest single-center series on LTx from DCD donors reported thus far. The experience of the group dates back to 1993, when Bob Love got interested and started the use of lungs from this type of donor in whom other organs, like the kidney, liver, and pancreas, were already recovered for transplantation at Madison.

The authors conclude that the long-term patient and graft survival in lung transplant recipients from donors after cardiac death are equivalent to those from donors after brain death and that these donors therefore could be safely used to expand the donor pool. Nevertheless, the reported doubled incidence of bronchial complications in these recipients might be a concern that should be further investigated.

I have 3 questions for the presenter that I will pose one at a time.

The authors define the WIT as the period between the withdrawal of life support, extubation, and the start of cold perfusion, on average about 30 minutes. In my opinion this definition is not entirely correct because in some donors spontaneous breathing continues after extubation and the blood pressure remains sufficient to perfuse the organs for a longer period of time, and therefore the lungs cannot be considered as being ischemic already. To compare results between different institutions across the world and to enter data in an international register, such as the one from the ISHLT, we should agree on the same definition of warm ischemia: either from cardiac arrest until cold flush perfusion or when the blood pressure in the donor decreases to less than 50 mm Hg. Therefore my question is this: Can the authors comment on this definition and also provide us with the exact time between cardiac arrest or electromechanical dissociation and the start of cold perfusion?

Dr Osaki. Thank you very much, Professor Van Raemdonck, for your kind comments and the question about the appropriate definition of WIT. Dr Snell and colleagues, the group from Australia, suggested in a recent publication that the definition of WIT should be considered as the interval between starting at a systolic blood pressure of less than 50 mm Hg and the initiation of cold flush preservation of the organs for controlled DCD donors. We agree with this definition. In our organ procurement organization, since 2006, the changes in hemodynamics from extubation to cardiac arrest are recorded. However, 15 of 18 cases DCD donor LTx were performed before that time, and the data were not documented. Thus we were not able to obtain records of the hemodynamic changes during the time between extubation and declaration of death on most DCD donors. In terms of the exact time between cardiac arrest and cold flush of preservation solution, the mean time was 9 minutes.

Dr Van Raemdonck. All donors were extubated in the operating room, and some donors were returned to the ward if cardiac arrest did not occur within 2 hours after withdrawal of support. Can the authors tell us what percentage of organs could not be recovered from these potential donors and whether they believe that any sedative drugs could be given to improve the donor's comfort and relieve the family from further awaiting the inevitable death in the hours thereafter?

Dr Osaki. During the study period, from January 1993 to April 2009, 269 DCD donor procurements were performed in our local organ procurement organization. From those, 18 DCD donor lungs were used, indicating a lung recovery rate of 6.7%. Although we tried, we could not identify the number of potential DCD donors in which cardiac arrest did not occur and were returned to the intensive care unit or hospital ward. In addition, the total number of DCD donor offers made to our program was not available from our database. In terms of care of DCD donor candidates, I cannot make any comments about the use of sedative drugs or end-of-life management for those DCD donor candidates; however, I am sure those were applied by the physicians managing the donor candidates.

Dr Van Raemdonck. Finally, the freedom from airway complications was significantly lower in recipients of organs from DCD donors. This raises the question of whether the additional warm ischemic interval contributes to the damage of the larger airways subjected to impaired healing. The use of an additional retrograde pulmonary flush delivered through the 4 pulmonary veins is believed to preserve the bronchial tree better through collateral perfusion of the bronchial arteries. Did your group at Wisconsin implement such a retrograde flush in your DCD donors, and if so, was this equally compared between both groups?

Dr Osaki. We appreciate your suggestion on a possible method to prevent airway complications in the DCD donor lung grafts. The possibility of increased airway complications deserves further investigation. About the specific question regarding the use of retrograde flush to the pulmonary veins, I can say that this has been part of our routine technique of lung graft recovery. In an animal study with a pig model, Binns and colleagues suggested that central airways might be more susceptible to the lack of perfusion during ischemia than lung parenchymal cells, which can maintain some aerobic metabolism through ventilation. Certainly the effects of warm ischemia on bronchial healing deserve further investigation.

Dr Van Raemdonck. Once again, I congratulate you on a nice presentation. Thank you.

Dr Love. Dirk, I can help with some of those question because in point of fact, none of the authors were involved primarily with any of these cases except for the case of bronchial dehiscence. That bronchial dehiscence, which I repaired myself, was a technical problem and not ischemia as reported here. None of the other bronchial problems in the initial 17 patients were a major problem for the patient and were managed bronchoscopically without significant morbidity.

The development of DCD donor LTx as a clinical reality during my tenure at the University of Wisconsin was adopted over many years. It has been gratifying to see the adoption of the techniques of donor management and selection, recipient selection, and validation of my results at many centers in Europe, North America, and Australia. Retrograde flush at procurement was used in all patients, and over the years, there was about 30% occurrence of nonretrieval of lungs when going out for procurement.

Dr Bryan F. Meyers *(St Louis, Mo)*. I think this is something that is a great idea in principle, but when it gets down to the specifics, it becomes more challenging to evaluate. When Dr Love started doing this, I am sure he was extremely selective about the DCD donors that he accepted and the interaction between the DCD donor and the risk of the recipient the lung was going into.

When I evaluate an offer from a potential DCD donor, I will weigh the quality of the donor lung and then look at potential recipients for one that is suitable. I also consider the distance and the likely length of ischemic time. There are a lot of factors that we have already put into the decision making that would help make this work out, and presenting this without knowing the bias behind all those careful selections would perhaps make this look equivalent when it is really not as equivalent as it might seem. I agree with more data collection to learn more about the decision making and the other unrecorded factors, but these are great results, and they make DCD donors appear equivalent, but I think that there were a lot of accommodations that were made to make DCD donors work out as well as possible in the beginning.

Dr John H. Dark *(Newcastle, United Kingdom)*. I would like to echo what others have said about the role of Bob Love in both originating this field and driving this particular series of patients forward.

My question is about the PGD incidence and the use of nitric oxide. You have clearly put a huge amount of work into collecting these data over the years. Your PGD incidence would perhaps seem a little higher than that been recorded in European and Australian series, although the numbers are all small. Was there any correlation between any of the preoperative variables in terms of WIT or cold ischemic time and PGD?

Dr Osaki. Thank you very much for your question.

Actually we did analyze the correlation between the WIT or cold ischemic time and the incidence of airway complications; however, there was no correlation between these parameters.

Dr De Oliveira. With regard to Dr Meyers' comments, before we start the indiscriminate use of DCD donor lungs, I think we have to be very careful because the definition of WIT is not yet very clear. It goes from a few minutes in countries in which euthanasia is allowed to as long as 90 minutes, as in one of the patients in our series. There is no question that there is a selection bias as well. Most DCD donor lungs meet standard criteria. I do not think there is that much experience about the use of extended criteria or marginal DCD donor lungs.

Having said that, I think this is an extremely important technique. In many situations I believe DCD donor lungs have been used as a salvage procedure, and I do not think those patients would have received a lung transplant on time if they had to wait for a BDD.

Finally, I think there is a lot of potential in the future to combine the use of the ex vivo lung perfusion system and the use of DCD donor organs. DCD donor organs could potentially be evaluated before LTx.

Dr Shaf Keshavjee *(Toronto, Ontario, Canada)*. If I can follow up on that, we have done about 11 or 12 DCD organ transplantations and because we have the ex vivo trial going, we have made it a policy to do ex vivo assessment of all of the DCD donor lungs in our program before implanting them to learn a little bit more about the process. DCD donor lungs in many cases could in fact be better organs and not exposed to the ravages of inflammatory injury of brain death and brain stem coning and so on, but on the other hand, if death or cessation of circulation occurs slowly, you can go through an agonal phase of low blood pressure and shock with the possibility of developing a shock lung. Therefore it might well be a less predictable organ source. I do think that the ability to be able to assess the lung before you implant it might help us to define which organs are going to be usable.

Dr Bartosz Kubisa *(Szczecin, Poland)*. Thank you for your nice presentation.

The good results that you have received with these donors, are they far away from those of the non–heart-beating donors? Can we also have the same good results in the future from the non–heart-beating donors? What is the time difference in the case of your donors and the patients when the heart actually stopped and the explantation of lungs is after an hour or 2 or a longer period of time?

To clarify, I understand you are referring to category I and II donors in whom cardiac activity has already stopped? I guess the question is this: Do you expect to get equivalently good results with Maastricht category I and II donors as you have achieved with the category III donors?

Dr Osaki. I do not think so.

Dr Keshavjee. I think that that is another area of interest; obviously Steen has looked at it, and Dirk Van Raemdonck and others have explored this area as well. Andres Varela in Madrid has performed transplantations in a number of patients. There is no doubt that the category I and II donor lungs have a much more significant PGD and a lower 1-year survival than what has been published worldwide with BDDs. Once again, those are lungs that have taken a bigger hit, and I think again that there might be some good organs in that group, but there is more variability, and that speaks again for the advantage of the ability to be able to test or recondition the lungs before you implant them.

Dr Waleed Saleh *(Riyadh, Saudi Arabia)*. You mentioned that the airway complications after DCD donor LTX were higher?

Dr Osaki. Yes.

Dr Saleh. What were they specifically, more dehiscence or stenosis or infection?

Dr Osaki. Actually, we had 5 airway complications. One had ischemic bronchial dehiscence on POD 8, but the other 4 patients had bronchial stenosis, and 2 of them had an *Aspergillus* species infection.

Dr Stephen D. Cassivi *(Rochester, Minn)*. I have a quick comment. I think Bob Love and his group are to be congratulated once more. This is especially true in this day and age of tremendous transparency in transplantation in North America and when in the United States every outcome is on the Internet within 6 months. In transplantation our outcomes are scrutinized very, very closely. This has a real potential to stifle innovation such as this. Therefore for Dr Love to move forward with something like this is a testament to his ability to take on risk and manage it successfully. Congratulations.

Dr Osaki. Thank you very much.

Dr Keshavjee. I think that is exactly what Tom Spray was alluding to in his Presidential Address. Congratulations again, Bob.